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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,078	06/16/2007	Herve Groux	0733-1001	1413

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EXAMINER	
JUEDES, AMY E	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
08/09/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

Office Action Summary	Application No.	Applicant(s)	
	10/579,078	GROUX ET AL.	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-32,37-41 and 44-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-32,37-41 and 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks, filed 6/8/10, are acknowledged.
Claims 1-28, 33-36, and 42-43 have been cancelled.
Claims 29, 31, 38-40, and 44 have been amended.
Claims 45-46 have been added.
Claims 29-32, 37-41, and 44-46 are pending and are under examination.

2. The rejection of the claims under 35 U.S.C. 102(a) as being anticipated by Foussat et al. is withdrawn in view of Applicant's declaration under 35 C.F.R. 1.132 filed 6/8/10.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31-32 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As set forth previously, Claim 31 specifics that the pharmaceutical formulation further comprises, as a combined preparation, the peptide antigen or a polypeptide comprising said peptide, to be administered prior to the topical administration of the lipopeptide. The recitation of a "combined" preparation appears to indicate that the formulation comprises a lipopeptide and a peptide in a single composition. However, claim 29 is already direct to a single composition comprising both a peptide and a lipopeptide. Furthermore, the claims also specify that the formulation is to be administered subcutaneously prior to the topical administration of the lipopeptide composition. Thus, it is not clear if the "combined preparation" might refer to two separate formulations, one comprising a lipopeptide for topical administration, and one comprising a peptide/polypeptide for subcutaneous administration. Therefore, the metes and bounds of the claims cannot be established. For the purposes of examination, claim 31 is being interpreted as single formulation comprising both a lipopeptide and a peptide/polypeptide.

Applicant's arguments filed 6/8/10 have been fully considered, but they are not persuasive.

Applicant argues that the amendment to the claims overcomes the rejection.

The claims are still drawn to a "combined preparation" comprising a lipopeptide

formulated for topical administration, and the peptide antigen, wherein the peptide antigen is to be administered in an immunization step prior to the topical application of the lipopeptide. It is unclear how a "combined preparation" can be administered in such a way that the lipopeptide portion is administered topically, while the peptide portion is administered by immunization. Thus, it is still not clear if the "combined preparation" comprises two separate formulations stored together, or whether the "combined preparation" comprises a single lipopeptide/peptide composition that is formulated in such a way that it is suitable for both topical administration and immunization.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 37-40 and 44 stand rejected, and claims 45-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A pharmaceutical formulation or cosmetic formulation comprising a lipopeptide and a topical/cosmetic carrier,

does not reasonably provide enablement for:

A pharmaceutical/cosmetic formulation comprising a lipopeptide and a topical/cosmetic carrier for treating or preventing a skin disease, diseases of the mucosa, chronic inflammatory disorders and autoimmune pathological disorders.

As set forth previously, The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature

of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The instant claims are drawn to a pharmaceutical composition comprising a lipopeptide, wherein said composition is effective for treating a broad range of diseases, including inflammatory autoimmune diseases, cancer, and infection. The instant claims encompass using the claimed compositions to treat conditions with widely different etiologies and pathological mechanisms. For example, treatment of autoimmune disease involves suppressing a pathogenic immune response, while treatment of infection or cancer involves inducing a protective immune response. The ability of a single treatment to be effective for such widely divergent diseases is highly unpredictable. Furthermore, lipopeptides are known to have an inflammatory adjuvant effect, enhancing the immune response to peptide antigens (see Le Gal et al.). Thus, while it might be possible to use a viral or bacterial peptide conjugated to a lipid to treat infection, or to use a tumor peptide conjugated to a lipid to treat cancer, the instant claims are not limited in this regard. Furthermore, the instant claims encompass using the claimed lipopeptides to treat autoimmune inflammatory disease, which would be highly unpredictable given the immune stimulating effect of lipopeptides.

Thus, given the breadth of the claims and the unpredictability of the art, the instant specification must provide a sufficient disclosure to enable one of skill in the art to use the compositions as broadly claimed. The instant specification demonstrates that a tumor peptide lipopeptide conjugate is effective in inducing an antigen specific TH1 immune response. However, the claims are not limited to a lipopeptide tumor peptide conjugate for treating cancer, but broadly encompass treating or preventing a myriad of diseases with any lipopeptide. The instant specification further demonstrates that a lipopeptide-OVA peptide conjugate is effective at stimulating adoptively transferred OVA specific regulatory T cells in vivo. However, no evidence is provided that a lipopeptide composition by itself (i.e. in the absence of co-transfer of regulatory T cells) is effective for treating or preventing autoimmune disease, as claimed. Thus, given the breadth of the claims, the unpredictability of the art, and the lack of guidance provided by the instant specification, it would require undue experimentation to use the lipopeptide compositions, as broadly claimed.

Applicant's arguments filed 6/8/10 have been fully considered, but they are not persuasive.

Applicant argues that based on the teachings of the instant specification, the skilled artisan would know how to select the right peptide for either priming CD8/CD4 T cells or Tr1 cells. Applicant particularly notes that Example 2 demonstrates that TRP2 or OVAa lipopeptide can prime CD4/CD8 T cells, as shown in Example 2, while OVA lipopeptide can activate adoptively transferred T regs, as shown in example 1.

As an initial matter, it is noted that the specification demonstrates the same peptide (OVA) can either induce regulatory T cells or stimulate inflammatory CD4 T

cells, depending on the circumstance. Thus, treating diseases as divergent as autoimmune disease or melanoma with a lipopeptide would be extremely unpredictable and dependent on the particular inflammatory milieu and combination of peptide selection. Furthermore, the specification does not provide guidance for selecting peptides that activate Tr1 cells, except for the experimental antigen OVA, which was only effective after adoptive transfer of OVA specific Tr1 cells. Thus, it would require undue experimentation to select lipopeptides effective for stimulating Tr1 cells for the treatment of the wide range of different diseases encompassed by the instant claims. Furthermore, as noted in the original rejection, it might be possible to use a tumor peptide conjugated to a lipid to treat cancer, the instant claims are not limited in this regard, and broadly encompass compositions comprising any lipopeptide that activates any T cells for treating cancers such as melanoma. The specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. As noted above, based on the unpredictability of the art, the breadth of the claims, and the lack of guidance provided by the instant specification, it would require undue experimentation to practice the full scope of the instant claims.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 29-32, 37-41, and 44 stand rejected, and claims 45-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Le Gal et al., 2002.

As set forth previously, Le Gal et al. teach a pharmaceutical composition comprising a lipopeptide and IFA (i.e. a water-in oil emulsion, see page 222and 224 in particular). The instant specification on pages 6 and 16 teaches that pharmaceutically topical acceptable carriers or cosmetically acceptable carriers include water-in-oil emulsions. Thus, the IFA of Le Gal et al. can be considered a pharmaceutically topical acceptable carrier or a cosmetically acceptable carrier, as recited in the instant claims. Le Gal et al. teach that the lipopeptide comprises peptides specific for a T cell population covalently coupled to a lipid group (i.e. a radical, see page 221-222, in particular). Additionally, said composition can be considered a "combined" preparation comprising the peptide. Le Gal et al. teach that the lipopeptide is capable of stimulating both CTL and T helper cells (i.e. CD8+ or CD4+ T cells,

see page 221 and 224, in particular). Le Gal et al. teach that the lipopeptide compositions can be used as a melanoma vaccine (i.e. to treat melanoma). Furthermore, said lipopeptide would inherently be capable of activating CD3+CD4+CD18brighCD49b+ cells, and treating inflammatory diseases or diseases of the mucosa, since it is he same as the composition of the instant claims. Additionally, the limitations of claims 30-31 wherein composition is to be administered topically/subcutaneously/intraperitoneally refers to an intended use of the claimed composition, and does not render the instant claims patentable in the absence of a structural difference.

Applicant's arguments filed 6/8/10 have been fully considered, but they are not persuasive.

Applicant argues that Le Gal et al. do not teach a carrier selected from the group consisting of emulsion carriers, anhydrous liquid solvents, oils, silicones, or aqueous-based single phase liquids, as recite din the amended claims.

Le Gal et al teach using a pharmaceutically acceptable carrier comprising an emulsion of water and IFA (i.e. a water in oil emulsion). The instant specification on page 6 teaches that emulsion carriers include water in oil emulsions. Thus the emulsion of Le Gal et al. is an "emulsion carrier" as recited in the instant claims.

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 8am to 4:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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